Evaluation of right ventricular function in patients with copd and its correlation with respiratory functions

COPD and right ventricle

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Abstract

Aim: In this study, we aimed to evaluate the right ventricle functions in COPD and to investigate its relationship with the stage of the disease and respiratory functions. Matrial and Method: This retrospective study was conducted in our Pulmonology and Cardiology clinics between December 2015 and 2016. Thirty-four patients with COPD (who did not show any evidence of cardiac failure), 21 healthy subjects were included in the study. The patients with GOLD stages 1 and 2 COPD were included in Group 1, while Group 2 included the cases of GOLD stages 3 and 4. For each participant, the medical files were reviewed and the following data were recorded: the BODE index and PFT parameters, left ventricle ejection fraction, systolic pulmonary arterial pressure (SPAP), systolic and diastolic dimensions of the right ventricle, tricuspid annular plane systolic excursion (TAPSE) and right ventricle myocardial perfusion index (Tei index). Results: The mean ages in the COPD and the control groups were 66.0 ± 9.0 and 51.7 ± 6.8 (p=0.001). Group 1 and Group 2 and analyzed, the advanced disease group showed significantly lower six-minute walk test results and significantly higher Tei index values (p=0.001 and p=0.040). TAPSE was found to be negatively correlated with CAT score and SPAP. Also, the Tei index was negatively correlated with the six-minute walk test and positively correlated with the BODE index. Discussion: COPD patients may show symptoms of right ventricle dysfunction depending on the stage of the disease. TAPSE and the Tei index, seem to be closely related to the functional status and prognosis in this patient population.

Keywords

Chronic Obstructive Pulmonary Disease; Echocardiography; Right Ventricle Dysfunction; Tei Index

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a preventable and treatable disease characterized by progressive respiratory symptoms and airflow limitation [1]. Numerous comorbid conditions bearing similar risk factors and systemic inflammation accompany COPD. These comorbidities may occur at any time during the disease and may significantly alter its severity and prognosis. The most commonly encountered and the most important one among these comorbidities are cardiovascular disorders [1-3]. They worsen the overall quality of life and survival rates of patients with COPD, being responsible for 20-25% of all COPD-related deaths. COPD leads to pulmonary hypertension and cor pulmonale via its effects on the pulmonary vessels and the right ventricle [4]. Therefore, cardiovascular parameters should also be evaluated in this patient population. Echocardiography is a fast and non-invasive method that can accurately evaluate the frequently affected functions of the right and the left ventricle in COPD [4,5].

There are many numbers of studies on the cardiovascular comorbidities that accompany COPD that investigates the relationship between these comorbidities and respiratory functions but the disease verity and COPD flare-up frequency are not clear. The aim of our study is to evaluate the right ventricle functions in COPD and to investigate its relationship with respiratory functions, the severity of COPD and incidence of attacks.

Material and Methods

Following approval of the local ethics board, the study was conducted as retrospective in our Pulmonology and Cardiology clinics between December 2015 and December 2016. A total of 34 male patients who were diagnosed with COPD according to clinical history, physical findings, imaging studies and pulmonary function tests (PFT), who did not show any evidence of cardiac failure and in whom echocardiography was performed were included in the study. The patients who were not able to cooperate with the PFT procedures or who were in an unstable COPD phase were excluded. A total of 21 healthy male subjects without any chronic conditions (i.e. COPD, cardiovascular problems, neurovascular problems and metabolic problems) who were admitted to the echocardiography laboratory were included in the control group.

Study Protocol

Medical files of all participants were evaluated in details, and the demographic data regarding age, occupation, smoking history, body mass index (BMI) and medical history were noted. Also, for each participant in the COPD group, PFT parameters, COPD assessment test (CAT) results and the BODE index result consisting of BMI value(B), the severity of airway obstruction (O), the severity of dyspnea (D) and exercise capacity (E) was recorded. Additionally, the Modified Medical Research Council (MMRC) dyspnea scale resultused for assessment of dyspnea severity and the number of attacks and hospitalizations over the past year were also recorded.

Pulmonary Function Tests (PFT)

All PFT evaluations were performed using a Jaeger Master Scope spirometer. Measurements were standardized as recommended by the American Thoracic Society [6]. COPD diagnoses were made according to the GOLD criteria (Global Initiative for Chronic Obstructive Lung Disease). A post-bronchodilator FEV1/FEVC ratio of <70% was considered as COPD. Post-bronchodi-

lator FEV1 values of ≥80%, 50%≤FEV1<80%, 30%≤FEV1<50% and <30% were classified as mild (GOLD stage 1), moderate (GOLD stage 2), severe (GOLD stage 3) and very severe (GOLD stage 4) COPD, respectively [1]. The patients with GOLD stages 1 and 2 COPD were included in Group 1, while Group 2 included the cases of GOLD stages 3 and 4.

Echocardiography

All echocardiographic assessments were run by a single experienced cardiologist using a General Electric VIVID S5 system and a 3 MHz probe. For each participant, the medical files were reviewed and the following data were recorded: left ventricle ejection fraction, systolic pulmonary arterial pressure(SPAP), systolic and diastolic dimensions of the right and left ventricles, tricuspid annular plane systolic excursion (TAPSE) and right ventricle myocardial perfusion index (RV-MPI = Tei index).

Statistical Analysis

Similar literature results and a prior power analyzes performed with the Chi-Square test showed that at least 44 individuals in total were required, with a total sample size of at least 22 individuals in each group. In this case, the power of the test > %80 was obtained. Statistical analysis of the data was performed using SPSS 20 (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0, Armonk, NY: IBM Corp.) statistical software package. The variables were represented as means ± standard deviation, percentages or frequency values, where appropriate. The prerequisite of variance homogeneity for the parametric variables was assessed with Levene's test. Shapiro-Wilk test was used to evaluate the assumptions of normality. Intergroup comparisons were made using the Student's t-test or the Mann-Whitney-U test, for the variables which met or did not meet the parametricity criteria, respectively. Categorical data were analyzed with the Fisher's Exact and the Chi-Square tests. When the expected outcomes were lower than 20%, the Monte Carlo Simulation method was used to estimate values for those outcomes to be included in the analysis. The relationship between the two variables was assessed by the Kendall Rank Correlation Test when the parametric test prerequisites were not met. P-values of <0.05 and<0.01 were accepted as statistically significant.

Results

A total of 55 participants, including 34 COPD patients and 21 healthy control subjects were evaluated in this study. All cases were male. The mean ages in the COPD and the control groups were 66.0 ± 9.0 and 51.7 ± 6.8, respectively (p = 0.001). In the COPD group (when it is aged as covariance), the BMI was 25.13 ± 3.89, and in the control group, it was 25.52 ± 1.83 (p = 0.675). Table 1 shows the demographic data, pulmonary function results, and the echocardiography findings. In the COPD group, 4 patients were in stage 1 (11.7%), 17 in stage 2 (50%), 9 in stage 3 (26.4%) and 4 in stage 4 (11.7%) according to the GOLD classification. All patients in the COPD group and five subjects in the control group (23.8%) had a smoking history (p=0.001). Eight COPD patients (23.5%) also had arterial hypertension, whereas none of the subjects in the control group had. Abbreviations: BMI: Body mass index. FEV1. forced expiratory volume in 1 second; FVC. forced vital capacity. SPAP: Systolic pulmonary artery pressure.

When the COPD patients were divided into Group 1 (GOLD stages 1 and 2) and Group 2 (GOLD stages 3 and 4) and ana-

Table 1. The demographic data. Pulmonary function test values and echocardiographic measurements in the patient and the control groups.

	COPD	Control	p	When it is aged as covariance p
	n=34	n=21		
Age (year)	66.0±9.0	51.7±6.8	0.001	
BMI (kg/m2)	25.13±3.89	25.52±1.83	0.675	0.442
Six-minutewalk test (m)	334.47±103.84	452.14±87.33	0.001	0.001
FEV1/FVC	53.38±12.77	78.87±5.2	0.020	0.001
FEV1 (%)	55.81±20.9	92.99±11.33	0.001	0.001
FVC (%)	81.01±18.89	95.35±15.99	0.006	0.001
SPAP (mmHg)	30.91±5.72	23.57±2.93	0.001	0.001
TAPSE	1.76±0.25	2.16±0.16	0.001	0.001
Ejectionfraction(%)	61.94±5.76	66.71±2.59	0.001	0.001
Left Ventricle Diastolic Diameter (mm)	34.88±4.57	30.9±2.64	0.001	0.001
Right Ventricle Diastolic Diameter (mm)	25.59±3.77	22.48±3.83	0.005	0.001
Tei Index	0.61±0.14	0.47±0.11	0.001	0.001

lyzed, the advanced disease group showed significantly lower six-minute walk test results and significantly higher Tei index values (p=0.001 and p=0.040, respectively).

As for the incidence of COPD exacerbations over the past year, in Group 1, five patients (23.8%) had one and 1 patient (4.76%) had three attacks whereas, in Group 2, two patients (15.3%) had one, 6 patients (46.1%) had two and 1 patient (15.3%) had three attacks. The results regarding the hospitalization frequency over the past year were as follows: 1 patient in Group 1(4.8%) had one course of hospitalization whereas in Group 2, four patients (30.8%) were hospitalized for once and two patients (15.4%) were hospitalized twice. Attack and hospitalization frequencies were found to increase as COPD stage advanced (p=0.004 and p=0.01, respectively).

No correlation was detected between the pulmonary function test parameters and echocardiographic measurements. TAPSE was found to be negatively correlated with CAT score and SPAP (r=-0.341, p=0.049 and r=-0.412, p=0.016, respectively). Also,the Tei index was negatively correlated with six-minute walk test results and positively correlated with the BODE index (r=-0.377, p=0.028 and r=-0.378, p=0.027, respectively) (Table 2).

Table 2. The correlations between the echocardiographic data and the functional parameters

Echocardiographicdata	Variables	r	P
TAPSE	SPAP	-0.412	0.016
	CAT score	-0.341	0.049
Tei index	Six-minute walk test	-0.377	0.028
	BODE index	0.378	0.027

Attack frequency over the past year had a negative correlation with six-minute walk test, whereas it was positively correlated with MMRC dyspnea score, CAT score, the BODE index and the Tei index (r= -0.794, p=0.000; r= 0.855, p= 0.000; r= 0.657, p= 0.000; r= 0.841, p= 0.000; r= 0.358, p= 0.038, respectively).

Hospitalization frequency, on the other hand, was found to be negatively correlated with six-minute walk test, whereas it was positively correlated with MMRC dyspnea score, CAT score and the BODE index (r= -0.666, p=0.000; r=0.741, p=0.000; r=0.442, p=0.009; r=0.762, p=0.000, respectively) (Table 3).

Table 3. Correlation analysis between the attack and hospitalization frequencies and the functional parameters and Tei index

Independent	Dependent	r	P
Number of attacks (over the past 1 year)	Six-minute walk test	-0.794	<0.001
	MMRC dyspnea score	0.855	<0.001
	CAT score	0.657	<0.001
	BODE index	0.841	<0.001
	Tei index	0.358	0.038
Number of hospitalizations (over the past 1 year)	Six-minute walk test	-0.666	<0.001
	MMRC dyspnea score	0.741	<0.001
	CAT score	0.442	0.009
	BODE index	0.762	<0.001

Discussion

Cardiovascular changes are the most commonly encountered extra-pulmonary complications of COPD due to systemic inflammation. Right ventricular dysfunction and pulmonary vascular changes are the most common two of such changes, and these are associated with survival in COPD [3,7]. Alpsoy and colleagues found in a previous study that while SPAP, diameter and free-wall thickness of the right ventricle were higher in COPD patients than the healthy subjects, the Tei index, on the other hand, was similar between the two groups [8]. Geyik et al. reported that COPD patients showed significantly lower TAPSE values, higher SPAPs and higher right ventricle systolic and diastolic diameter measurements [9]. Our results were in accordance with the previous reportsthat TAPSE values as an indicator of right ventricle dysfunction were detected to be lower and SPAP, Tei indices, and right ventricle systolic and diastolic diameters were higher in the COPD patients.

The main functional assessment and mortality prediction parameters in COPD are six-minute walk test, MMRC dyspnea score, CAT score and the BODE index [1]. When intergroup comparisons were made between the patient subgroups (i.e. Group 1 which includes GOLD stages 1 and 2, and Group 2 which includes GOLD stages 3 and 4), it was found that the parameters mentioned above were significantly lower in the cases with advanced stage. In echocardiography, we identified that, among the markers of right ventricular function only the Tei index was significantly higher in the advanced cases. The Tei index is easily measured by echocardiography, is well correlated with tricuspid failureand indicates right ventricular damage [5,10].

TAPSE and the Tei index, the two markers of right ventricular dysfunction, are accepted to be closely associated with disease progression and overall quality of life. Caminiti and colleagues in their study evaluating the relationship between exercise intolerance and right ventricle functions in COPD, demonstrated that TAPSE was positively correlated with six-minute walk test and was an independent indicator of pulmonary functions [11]. In a similar study, Tannus-Silva et al. underscored that the Tei index was not only positively correlated with the BODE index but also was closely associated with deterioration in the quality of life [10]. Burgess and colleagues concluded that the Tei index is an important prognostic marker [12]. Our results revealed that TAPSE is negatively correlated with CAT score and SPAP and that the Tei index is negatively correlated with six-minute walk test results and positively correlated with the BODE index. These findings altogether suggest that both parameters are closely associated with disease progression.

Our results demonstrated no correlation between PFT parameters and echocardiographic measurements. In a study by Das et al., which evaluated right ventricular dysfunction in COPD, SPAP, and the Tei index were found to be negatively correlated with FEV1, FEV1/FVC, PEF and FEF25-75 [5]. The BODE index,

which is constituted by BMI (B), the severity of airway obstruction (O), the severity of dyspnea (D) and exercise capacity (E) is a better predictor of prognosis than when its components are evaluated separately. We found a negative correlation between the BODE and Tei indices, which is suggestive that the BODE index not only is a predictor of prognosis but also may be negatively correlated with pulmonary functions.

The number of exacerbations and hospitalizations over the past year are other parameters associated with the progression of the disease in COPD, and both affect the overall quality of life, functional status, and survival of the patients. In their study, Tanaka and colleagues underlined that right ventricular dysfunction affects daily activities in COPD and is related to the prognosis of the disease; they suggested the Tei index as an indicator of right ventricular function. In the same study, the Tei index was found to be positively correlated with the MMRC dyspnea scores, overall survival rates and hospitalization frequency [13]. Similarly, our study also revealed a positive correlation between exacerbation rates and the Tei index.

The first limitation of our study is the limited number of patients. Another limitation is that the average age of the study and control group is not similar. However, the age factor was eliminated by covariance analysis. Echocardiographic parameters to assess pulmonary pressures and right ventricular functions are load-dependent. The lack of load-independent parameters is another limitation of the study. The strength of the present study is that a single expert investigator recruited and appraised patients and performed all PFT and echocardiographies, thus reducing analytical variability.

Conclusion
COPD patients may show symptoms of right ventricle dysfunction depending on the stage of the disease. The parameters of right ventricle function, particularly TAPSE and the Tei index, seem to be closely related to the functional status and prognosis in this patient population.

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